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EXAMINER	
MARVICH, MARIA	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/774,122	ZWAKA ET AL.	
	Examiner	Art Unit	
	MARIA B. MARVICH	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-21* is/are pending in the application.

4a) Of the above claim(s) *5,6,11 and 14-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,7-10,12, 13, 17 and 18-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1 and 3-21 are pending. Claims 5, 6, 11 and 14-16 are withdrawn. Therefore, claims 1, 3, 4, 7-10, 12, 13, 17 and 18-21 are under examination in this action.

It is noted that Prasad et al while included on the 892 mailed 9/25/09 is not associated with the file. Therefore, a copy is forwarded with this action.

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Claim Objections

Claims 1, 3, 4, 7, 8 and 12 are objected to because of the following informalities: Claim 1 appears to have the phrase "on an insert" inadvertently inserted in line 8-9. Otherwise, it is unclear why this phrase is present as the claim recites, the construct comprises a marker gene for cellular identification in an insert". The marker is present on a construct and it is not clear how it is also on an insert.

Claims 1, 7 and 17 have been amended to overcome previous objections, however, to be complete it would be remedial to amend the phrase "an ES cell genome" to --the ES cell genomes-- for proper antecedent basis. As well, the phrase "the stem cell genomic regions" as --the ES cell genomic regions--.

Each of the dependent claims 3, 4, 8-10 and 13 should be amended to recite --The method of claim --. When referring to previous claims, it i proper to use the article "the" as opposed to "a".

The amendment to claim 3 has not clarified the method step encompassed therein completely. At issue is the order of events. As recited, the claim states that upon recombination the marker is operably linked to a specific promoter. However, this is not necessarily the case.

Rather, cells are selected that express the marker in a desired state of differentiation can be identified. More specifically, --wherein the construct does not comprise a promoter operably linked to the marker and following recombination cells that express the marker gene in a desired state of differentiation are isolated due to operable linkage of the marker with the differentiation specific promoter in the genome--.

Claim 12 repeats several steps from claim 7 which confuses the purpose of claim 12. As further explanation it is noted that the claim recites "purifying cells of a defined lineage obtained from human embryonic stem (ES) cells" is confusing. It is unclear if these are cells of "the defined lineage of claim 7" or another lineage altogether. The steps suggest that the method is --purifying cells of the defined lineage of claim 7 from a culture of ES cells-- wherein the method requires --a) identifying genes selectively expressed in the defined lineage--. As recited, the claim refers to a number of overlapping as well as non-overlapping cells and conditions that require clarification in order for the claim to be understood.

For simplicity and hence clarity, claims 19-21 should be amended to recite, --wherein the electroporation is a single 320 volt, 200 microfarad pulse--.

Appropriate correction is required.

Claim 13 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 12 recites that the cells of a defined lineage are purified

following their differentiation. Claim 13 improperly recites that these cells are undifferentiated. Hence, this is a species of cells that is not encompassed by the species recited in claim 12.

Response to Argument

Applicants' arguments filed 1/25/10 have been fully considered but they are not persuasive. Applicants argue that multiple copies of the construct can be introduced but they only recombine with one stem cell genome of that cell. However, the claim recites use of multiple cells for recombination as well as identification of cells and hence there are multiple genomes that belong to the multiple cells. Hence, the claims are not using a single cell. By reciting one genome, applicants are inconsistent in claim construction. In other words, cells are electroporated, recombination occurs in a cell and then cells are identified which is inconsistent. The issue with claim 12 has been clarified above. It is clear that applicants intend on using the purified cells of claim 7 to identify genes associated with this lineage and to furthermore use these genes to identify other cells with similar lineage. However, the claims refer to a number of overlapping cells with no indication as to their relationship with one another. For example, are the cells of defined lineage of claim 12 related to the lineage of claim 7. They must as the genes from the defined lineage of claim 7 cannot be used to identify any other type of cell. However, this relationship is missing in the claims. As well, it is not clear what is meant by obtained from human embryonic stem (ES) cells. It is noted that once this abbreviation has been stated in claim 1 there is no need to repeat it in other claims. Hence, ES cells can be used in place of embryonic stem cells in all of the claims absent claim 1. As to claim 13, applicants argue that the genes can be used by a person of skill. However, the objection is not based upon the language related to the

genes but to recitation that the cells are undifferentiated. This cannot be as claim 12 recites explicitly that the cells are differentiated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4, 7, 8, 10, 12, 17 and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al (US 6,146,888; see entire document) in view of Thomson et al, Science, 1998, pages 1145-1147 or Jaynes et al (US 6,303,568; see entire document) or Chalitta-Eid (US 7,135,549; see entire document) as evidenced by Tenner et al (US 5,965,439; see entire document) or Tajima et al (PNAS, 1998, ; see entire document) further in view of Prasad et al (In Vitro Cell Dev Biol Anim. 1994 May;30A(5):321-8) and Takada et al (Cell Transplant. 2002;11(7):631-5). **This rejection is maintained for reasons of record in the office action mailed 9/25/09.**

Applicants claim a method of introducing a targeting vector comprising a marker gene into clumps of hES cell by electroporation in culture medium for homologous recombination.

Smith et al teach use of a targeting construct to be used in homologous recombination wherein the construct is introduced into the cell by transfection. Contemplated cells are human embryonic stem cells. The vector is shown in figure 3 and comprises 5' and 3' flanking arms for

homologous recombination as well as a marker to be selectively targeted to human ES cells (see e.g. bridging ¶, Col 1-2). The marker comprises a promoter that is selectively active in specific cell types (see e.g. claim 11). By transforming the cell with the marker construct and allowing homologous recombination to occur, cells can be purified that selectively express the marker such as by FACS (see e.g. col 3, line 60-65).

However, Smith does not explicitly teach the steps of electroporation. Hence, the step of electroporation of clumps of cells in culture media wherein the method requires 320V and 200 microfarad is not explicitly stated.

However, the art teaches that hES cells are cultured as clumps (see Thomson et al, reference 16). Furthermore, methods of electroporation of cells at the time of filing required use of cell clumps (see Prasad et al). Hence, use of clusters of cells is not advancement in the art. Hence, the question is does use of culture media in the electroporation method of the instant claims advance the state of the art. Jaynes et al teaches that electroporation is used to introduce DNA into a cell and is performed in culture medium (bridging ¶ col 6-7). In fact, Jaynes et al teaches use of this method for transfection of animal embryonic cells (see e.g. col 5, line 45-55). Challita-Eid teaches electroporation of ES cells using electroporation in culture medium. Furthermore, the method uses targeting vector with homologous arms (see e.g. col 35, line 1-35), which as evidenced by Tenner et al requires culture medium (see col 23-24, bridging ¶). Finally as regards claims 19-21, Tajima et al teaches electroporation using a single pulse of 320 V and 250 microfarads (page 11904, col 1, ¶ 4).

In KSR International Co. v. Teleflex lnc., 82 USPQ2d 1385 (U.S. 2007), the Supreme Court particularly emphasized "the need for caution in granting a patent based on a combination

of elements found in the prior art," (Id. At 1395) and discussed circumstances in which a patent might be determined to be obvious. Importantly, the Supreme Court reaffirmed principles based on it precedent that "[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." (Id. At 1395.)
In the instant case, Smith et al teach use of electroporation but do not provide the details to do so. Smith et al is directed to introduction of targeting vectors into embryonic stem cells wherein the vector is transfected into the cell by methods that include electroporation. At the time of the invention, electroporation was a well known method that was performed by application of electrical currents to cells wherein the cells were in culture medium. Without the culture medium, the cell would have not survived the electrical current. PBS has never been shown to be a superior method of electroporation. Furthermore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use culture medium in the method of electroporation taught by Smith et al because Smith et al teach that it is within the ordinary skill of the art to use electroporation to introduce DNA into cells and because Jaynes et al and Challita-Eid in view of Tenner et al teach that it is part of the method to use culture medium. Tajima et al teaches that it was known to use a single pulse at 320V and 250 mF. One would have been motivated to do so in order to receive the expected benefit of protection of the cells during transformation. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Furthermore, the MPEP teaches, "When the prior art discloses a range which touches or overlaps the claimed range, but no specific examples falling within the claimed range are

disclosed, a case by case determination must be made as to anticipation. In order to anticipate the claims, the claimed subject matter must be disclosed in the reference with "sufficient specificity to constitute an anticipation under the statute." In fact, the MPEP 2144.05 teaches, "a prima facie case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties. Titanium Metals Corp. of America v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985)." Furthermore, the MPEP teaches that optimization of ranges through prior art conditions or through routine experimentation is "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." (MPEP 2144.05II). In this case use of clusters of cells in culture media is taught by the art.

The MPEP (2145) also teaches that "The Hoeksema court further noted that once a prima facie case of obviousness is made by the PTO through citation of references, the burden is on the applicant to produce contrary evidence establishing that the reference being relied on would not enable a skilled artisan to produce the different compounds claimed. Id. at 274-75, 158 USPQ at 601. See also Ashland Oil, Inc. v. Delta Resins & Refractories, Inc., 776 F.2d 281, 295, 297, 227 USPQ 657, 666, 667 (Fed. Cir. 1985) (citing Hoeksema for the proposition above); In re Grose, 592 F.2d 1161, 1168, 201 USPQ 57, 63-64 (CCPA 1979) ("One of the assumptions underlying a prima facie obviousness rejection based upon a structural relationship between compounds, such as adjacent homologs, is that a method disclosed for producing one would provide those skilled in the art with a method for producing the other... Failure of the prior art to disclose or render obvious a method for making any composition of matter, whether a compound

or a mixture of compounds like a zeolite, precludes a conclusion that the composition would have been obvious."). In this case, the methods provide details omitted in the teachings of Smith et al wherein Tajima et al teach a method of electroporation wherein the conditions are similar and the differences do not appear to significantly alter the final method. Since, the methods are merely variants of one another, one would not conclude that the instant vector requires an inventive step over the prior art.

Claims 3, 9, 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al (US 6,146,888; see entire document) in view of Jaynes et al (US 6,303,568; see entire document) or Chalitta-Eid (US 7,135,549; see entire document) as evidenced by Tenner et al (US 5,965,439; see entire document) as applied to claims 1, 4, 7, 8, 10, 12, 17 and 18 above, and further in view of West et al (US 2004/0219563; see entire document). **This rejection is maintained for reasons of record in the office action mailed 9/25/09.**

Applicants claim a method of introducing a targeting vector comprising a marker gene into a cell by electroporation for homologous recombination wherein the vector does not comprise a promoter and wherein the cells are further differentiated following selection.

The teachings of Smith et al in view of Chalitta-Eid or Tenner are as above except the references do not teach that the construct is promoterless or that the cells are differentiated following transformation.

In ¶0180, West et al state that DNA markers can be inserted into human genes by homologous recombination. The markers are either inserted into sites so that they are transcriptionally regulated by the promoters of the genes into which they are inserted (see e.g.

¶0131) or comprise exogenous promoters that are development stage specific promoter/regulatory elements (see ¶0199). In these methods it is preferable to use homologous recombination for insertion of the construct comprising a marker into a specifically selected site in a gene that is conditionally expressed in a differentiating cell to disrupt and inhibit expression of the endogenous gene to produce a knockout or inserted to be transcribed ¶0073. The method of West et al allows for isolation of cells in distinct differentiated states such that the gene profile can be determined (see e.g. ¶0199).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use targeting vectors lacking promoters as taught by West et al in the methods of homologous recombination as taught by Smith et al because West et al teach insertion of a promoterless marker into the genome in a sight that is regulated by the stage of differentiation and Smith et al teach that it is within the ordinary skill of the art to transform a hES by electroporation with markers to identify transformed cells. Methods of inserting heterologous sequences into sequences comprising endogenous regulatory sequences were well known in the art and one would have been motivated to insert a promoterless marker into the genome in order to receive the expected benefit of using regulatory sequences known to work in the transformed cell. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Argument

Applicants' arguments filed 1/25/10 have been fully considered but they are not persuasive. The present rejection under 35 USC 103 is designed to assess whether use of clumps of cells for electroporation by a single pulse at 320V and 250 μF is an advancement of the art and specifically whether one would have, apprised of the art, performed the method of Smith et al of electroporating hES cells by use of clumps of the cells with conditions of a single pulse at 320V and 200 mF. The art teaches explicitly that human ES cells can be electroporated (Smith et al). Smith, however, does not provide explicit details regarding the method of electroporation. Turning to what was known about electroporation at the time of filing, the art teaches 1) use of clumps of cells (Prasad), 2) use of culture medium for ES cells (Jaynes et al and Challita-Eid in view of Tenner et al and Tajima et al) and 3) use of conditions for ES cells included a single pulse at 320V and 250 μF (Tajima et al).

Applicants have argued that the Prasad teaches electroporation of rat parotid clumps or single cells but does not teach electroporation of hES, that Thomson does not teach culturing or electroporation of hES in clumps or that Tajima does not teach ranges but simple use of 250 uF not 200uF. As an initial point, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413,208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). That Prasad teaches use of clumps but not use of clumps of hES cells ignores that the rejection is based upon a combination of references provided to show the state of the art at the time of filing. In this case, the claims recite a number of conditions that are not explicitly reported in a number of the references. Electroporation is a method that can be performed under

a number of conditions i.e. in culture medium or PBS and at a variety of different electrical conditions. For example, Prasad et al teach use of clumps of cells wherein medium is used.

> These clumps were transfected with plasmid vectors pSV3 and pSV by electroporation and calcium phosphate-Co-DNA-precipitation techniques. The untransfected and transfected cellular clumps were plated in precoated dishes containing modified MCDB-153 medium. Epithelial cells grew from the clumps that were attached.

Furthermore, turning to the art of human ES cells at the time of filing and what was known about these cells, the art teaches that the cells were known and methods of culturing and using were known. Thomson et al is explicitly directed at methods of culturing and handling human ES cells. One particularly relevant passage teaches,

> "Thirty-six fresh or frozen-thawed donated human embryos produced by IVF were cultured to the blastocyst stage in G1.2 and G2.2 medium (*25*). Fourteen of the 20 blastocysts that developed were selected for ES cell isolation, as described for rhesus monkey ES cells (*5*). The inner cell masses were isolated by immunosurgery (*26*), with a rabbit antiserum to BeWO cells, and plated on irradiated (35 grays gamma irradiation) mouse embryonic fibroblasts. Culture medium consisted of 80% Dulbecco's modified Eagles medium (no pyruvate, high glucose formulation; Gibco-BRL) supplemented with 20% fetal bovine serum (Hyclone), 1 mM glutamine, 0.1 mM b-mercaptoethanol (Sigma), and 1% nonessential amino acid stock (Gibco-BRL). After 9 to 15 days, inner cell mass derived outgrowths were dissociated into clumps either by exposure to Ca21/Mg21-free phosphate-buffered saline with 1 mM EDTA (cell line H1), by exposure to dispase (10 mg/ml; Sigma; cell line H7), or by mechanical dissociation with a micropipette (cell lines H9, H13, and H14) and replated on irradiated mouse embryonic fibroblasts in fresh medium. Individual colonies with a uniform undifferentiated morphology were individually selected by micropipette, mechanically dissociated into clumps, and replated. Once established and expanded, cultures were passaged by exposure to type IV collagenase (1 mg/ml; Gibco-BRL) or by selection of individual colonies by micropipette. Clump sizes of about 50 to 100 cells were optimal. Cell lines were initially karyotyped at passages 2 to 7."

This passage teaches that from single colonies, clumps were obtained provides detailed methods to do so. In fact, Thomson teaches that for use, clump sizes of 50-100 cells are optimal. Hence, looking to the art for methods of culturing and using human ES cells, one would have found that plating as clumps is preferable.

Jaynes et al teach that methods of electoporation of ES cells are best in culture medium. The details of the electroporation are vague but include a single pulse at a voltage between 100-400 V.

> The technique of electroporation, while known and used primarily in plant cell work, has also been applied to animal cells recently. The electroporation process depends on the discovery that in culture medium containing DNA fragments or genes desired for insertion, the application of an electric field causes the cells to become more porous to entry of the foreign genes, some of which will be incorporated into the cell genome and express the gene products. In a culture containing 1.times.10.sup.6 to 10.sup.7 cells, about one cell in a thousand actually incorporate the foreign DNA or genes, providing a sufficient concentration of the desired genes is present. Using a selectable marker aids identification and separation of cells incorporating the desired DNA for subsequent use.
>
> In a similar manner, mammalian or animal cells are electroporated, except that a greater number of cells are available, e.g., from about one hundred thousand to about one million cells can be placed in the treating chamber of the electroporator, and an increased pulse duration of 7 milliseconds or more at voltages from 100-400 volts. Additionally, if the foreign or antimicrobial gene is fused to a marker or selectable gene, such as a neomycin-resistance gene, after electroporation the treated cells can be cultured in a selection medium in which only transformed cells expressing the foreign gene will survive. Thus, insuring the transfer to an animal of active cells containing genes expressing one or more of the antimicrobial agents.

Chalitta-Eid et al and Tenner et al also teach methods of electroporation of the same cells. Tenner exemplifies methods of so doing which involve use of culture medium wherein a single pulse is provided. The cells are cultured similarly to those of Smith et al hence one would assume these cells to be formed as clumps. This pulse is 230 mV and 500 uF.

> Pluripotent J1 ES cells derived from the inner cell mass of 129/Sv blastocysts are cultured under standard conditions (Li, et al., Cell 69: 915-26, 1992). Approximately 1.times.10.sup.7 cells are transfected with 10-20 .mu.g of linearized construct by electroporation at 230 mV, 500 .mu.F using a Bio-Rad Gene Pulser and are replated on a feeder layer of .gamma.-irradiated G418-resistant primary mouse embryonic fibroblasts in Delbecco's modified Eagle's media supplemented with 5% FBS, 0.1 mM non-essential amino acids, 0.1 mM .beta.ME and 1000 U/ml leukemia inhibitory factor (Li, et al., Cell 69: 915-26, 1992).

Tajima et al teach

> Three x 107 ES cells in 0.8 ml of PBS were electroporated with 40 ug of linearized targeting construct in a 0.4-cm Bio-Rad cuvette with a single pulse at 320 V and 250 uF. After 24 hr, the medium was supplemented with 400 mg/ml of (3418 (GIBCO), and after 6-7 days, 200--300 ES clones were isolated from each electroporation.

Hence, the art indicates that the current at which electroporation occurs is not a precise requirement but has a great deal of tolerable range. Furthermore, it is not evident that there exists a functional or inventive difference between specifically Tajima and the instant conditions given that both use a single pulse on ES cells that constitutes the same voltage with minor variation in uF. The MPEP 2144.05 teaches, "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." Applicants have not that use of the details known in the art would not have been possible or that there is a significant difference between 200 and 250 uF.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARIA B. MARVICH whose telephone number is (571)272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Maria B Marvich, PhD
Primary Examiner
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